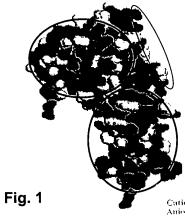
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Erythropoietin receptor (EPOR) hormone binding domain

amino terminal domain



hormone binding pocket

carboxyl terminal domain

Cationic/Basic Anione-Acidic Polar Uncharged Backbone hydrophobic are oil-like, they shun water basic are positively charged acidic are negatively charged polar uncharged are like water or alcohol backbone are the polymer chain

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Erythropoietin (EPO)

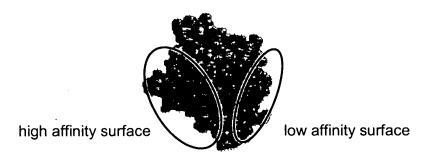


Fig. 2

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The initial event is the association of the high affinity surface of an EPO molecule with the hormone binding pocket on an EPOR.

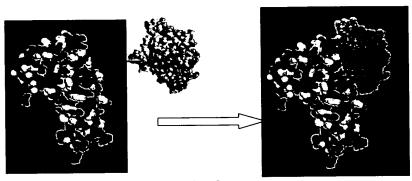


Fig. 3

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The EPORs are anchored in the membrane, they can only diffuse laterally or rotate in the plane of the membrane.

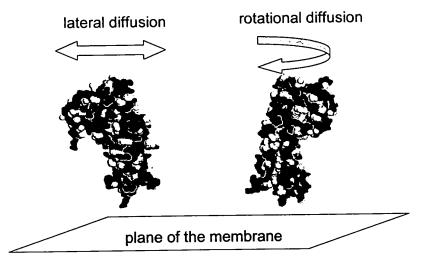


Fig. 4

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Once the high affinity EPO surface binds to the first EPOR, the low affinity EPO surface is positioned within a narrow two-dimensional plane. Because the unoccupied EPORs can only diffuse laterally or rotate in that narrow plane, they can easily engage low affinity EPO surface, forming the activated complex.

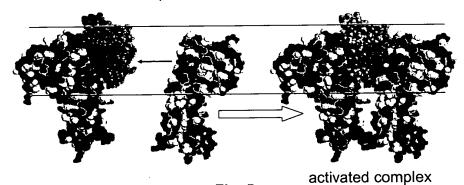


Fig. 5

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LZHRs are short helical peptides with one face of the helix composed of the amino acid leucine (grey), which has a hydrophobic (water-avoiding) side chain.

When two LZHRs are in close proximity the two leucinefaces "zip" together (right), to be shielded from water.

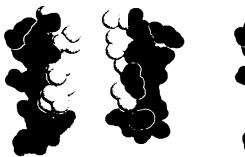




Fig. 6

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By attaching a short LZHR to the EPOR by a flexible linker peptide, the formation of the EPOR*-EPO-EPOR* complex can be effectively achieved in a cell-free environment.

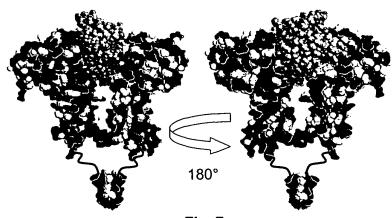


Fig. 7

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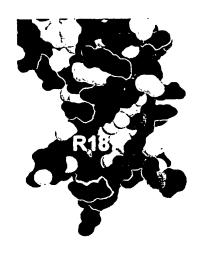




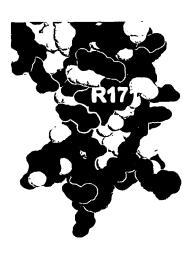


FIGURE 8

FIGURE 9

FIGURE 10





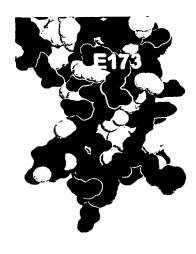
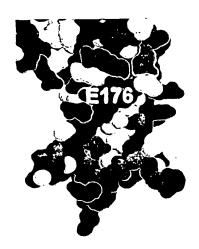


FIGURE 11

FIGURE 12

FIGURE 13

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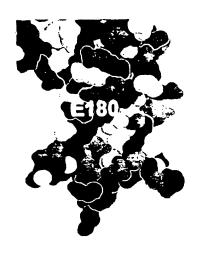


FIGURE 14

FIGURE 15

FIGURE 16

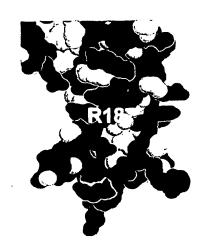


FIGURE 17